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# Adverse Drug Reactions and Safety Profiles in Cardiovascular Drug Therapy: A Pharmacovigilance Analysis

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***Authors' contributions***

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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## ABSTRACT

**Aims:** The purpose of the study is to identify adverse drug reactions (ADRs) and evaluate patient knowledge of the disease using the Knowledge Assessment Questionnaire (KAQ). This study was designed to compare adverse effects on Cardiovascular Drug Therapy. Adverse drug reaction (ADRs) is a major cause of mortality worldwide. The objective of the present study were a) to find out the prevalence of adverse drug reaction (ADRs) in the hospitalized patient by active surveillance, b) to study the profile of ADRs detected. (3) This study was done in superspecialty hospital Netaji Subhash Chandra Bose medical college & Hospital, Jabalpur, for three month study.
**Methodology:** This study was Pharmacovigilance group, belonging to department of cardiology at

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Netajisubhash Chandra bose medical college, Jabalpur M.P. (5) Total number of patients taken for study was 90 in number.

**Results and Conclusion:** Total 90 subjects were recruited in the study. Drug used for their co morbidities to find out ADRs in which maximum ADRs found in chronic rheumatoid heart diseases, for this diseases patient took in two combination mainly Digoxin with Clopidogrel (47.36%) and another were with atorvastatin, spironolactone and warfarin (47.30% ADRs Adverse drug reactions on particular body system were mostly observed on CNS (32.14% ADRs). According to Naranjonaranjo causality assessment scale applied to this study illustrates that the maximum possible and probable adverse drug reaction were shown on Furosemide as well as for Digoxin and Spironolactone.

*Keywords: Adverse drug reaction; pharmacovigilance; prospective; observational; cardiovascular.*

## 1. INTRODUCTION

Drugs are two-edged swords: while they can save lives, they can also result in adverse drug reactions (ADRs), which can be fatal. Globally, ADRs are a leading cause of illness and mortality. Hypertension is a chronic disease. The most prevalent cardiovascular condition and major public health issue is hypertension. [1, 16] As people age, the prevalence of hypertension rises; approximately 50% of those in their 60s and 70s have the condition. 90% of cases have an idiopathic cause. Approximately 81.5% of individuals with hypertension are aware that they have the condition, and 74.9% are receiving treatment with an antihypertensive medication.[5] Experts in the medical field who have previously treated patients with hypertension predict that by 2023,one-third of the population will have the condition, making it a pandemic [1,17]. Pharmacovigilance has been defined as “The science and activities related to detection assessment understanding & prevention of Adverse reactions and any other drug-related problem. [2,7]. The thalidomide disaster in 1961 awakened a need to regulate pharmacovigilance not only by the national competent (regulatory) authorities but also over and above this at an international level. The Sixteenth World Health Assembly in 1963 adopted a resolution stressing the need for early action in regard to rapid dissemination of information on adverse drug reactions and led to initiation of the WHO Pilot Research Project form International Drug Monitoring in 1968 [2,13]. The purpose of this was to develop a system, applicable internationally, for detecting previously unknown or poorly understood adverse effects of medicines forming the basis of the practice and science of pharmacovigilance to improve the safe and cost effective use of medicines by avoiding further disasters in both developed and developing countries in the interests of improved public [3,8,14].

### 1.1 Aim and Objectives

This study aim to reduce the intensity of undesirable effects produced by drug interaction as well as other negative responses related to the use of medicine through the marketing, distribution, prescription, distribution, and use of medicine in hospital. study involving prospective cross sectional study which is designed in Figure No. Objectives of this study was 1) to evaluate patient medication and find out our potential relavent ADRs 2)to estimate the rate and extent of potential ADRs in in-patient admitted during the study 3)to estimate the risk associated with potential ADRs 3) to identify the drug most commonly responsible for potential ADRs 4) to determine the cause including morbidity caused of this ADRs [4,9,15].

## 2. MATERIALS AND METHODS

This study was done in the Pharmacovigilance group at department of cardiology at Netaji Subhash Chandra Bose medical college &high tech superspeciality hospital Jabalpur.This study protocol was approved by NSCB Institutional Ethics Committee. Institution ethics committee reference no-IEC/2024/4355.

In a specified population at a particular point in time, a cross-sectional study characterizes the pattern of health-related events/factors and investigates the association between disease and different risk or protective factors of interest where cross -sectional study was according to world health organization guidelines [7,10,12].

### 2.1 Design

A prospective cross-sectional study was conducted of patient aged between 14 to 70 year who presented for the treatment and care to the

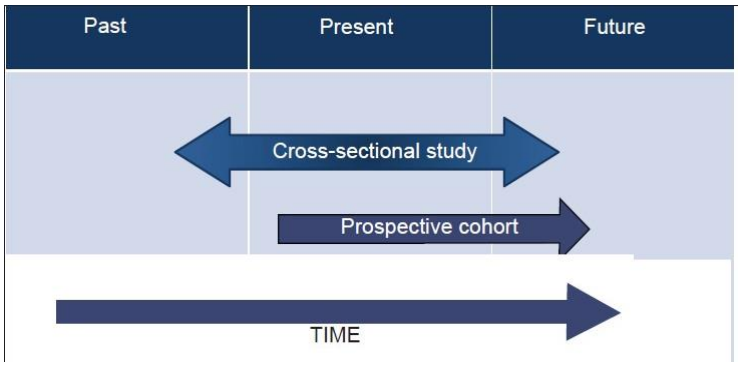



**Fig. 1. Design of present study- Prospective cross sectional study**

Netaji Subhash Chandra Bose medical college & high tech superspeciality hospital Jabalpur over a period of four month.

All the members of the families were first briefed about the project and verbal consent was obtained from each of the family member. Details of participants namely name, age, sex, residence, socio-economic status, consumption of drug, disease, laboratory values, status, co morbidities, eating habits, diagnostics value, medication chart, and previous detail adverse drug reaction if any were collected on a validated semi-structured questionnaire.( past treatment & clinical details were obtained from the medical records), data on treatment employed and complaints presented by patients during hospitalization [4,3,11]. Prospective cross sectional study was done for four months, and the number of patient included in this study was 90.

## 2.2 Origin/Source

Patient attended in in-patient department of cardiology and admitted in different unit of department of medicine of NSCB, Jabalpur. All data collected were coded as per variables and data sheet and analyze.[2,7] For the detection of possible ADRs the algorithm Naranjo et al.(1981) was used which involves the algorithm employs ten questions and yield a score for classification of causality of ADRs. Co morbidities were differentiating when there was a possible diagnosis in the patient charts.[8]

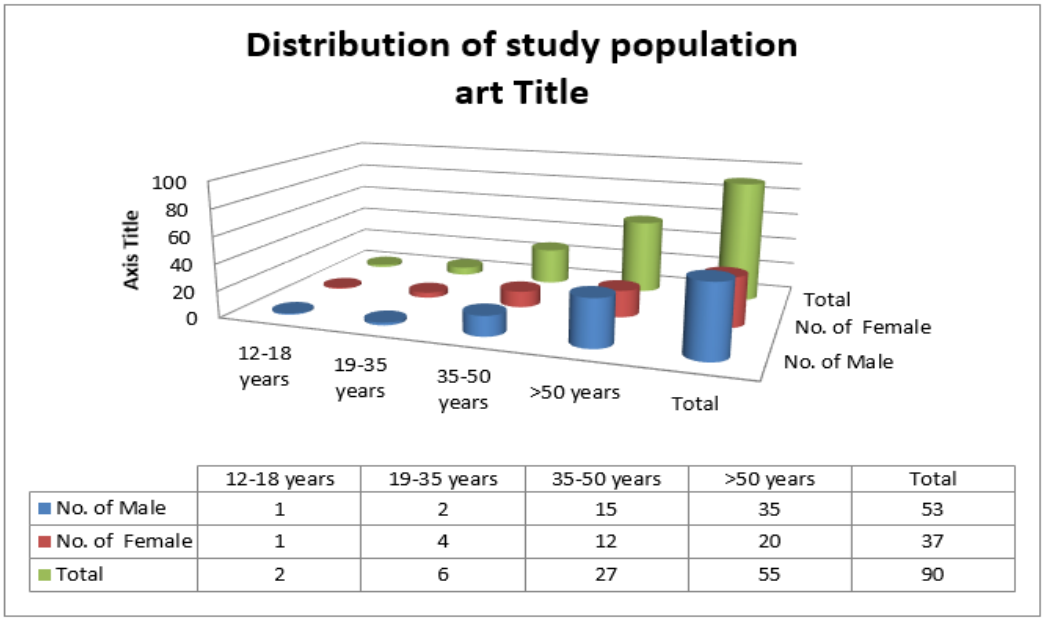
## 3. RESULTS

Total number of patients taken for study was 90 in number. From many criteria's which was included firstly on the basis of gender were 53 males and 37 females. Second on the age group, more than 50 year was 35 and 35-50 were 15. Distribution of population in study is designed in Fig. 2. The patients were looked upon for various comorbidities patients may have which may sensitize a patient and thus make prone towards the vicinity to face unpredictable ADRs occurring with the original ailment intended drugs. The distribution is thus helpful to indicate the propensity of possible ADRs which should be consciously monitored in a Pharmacovigilance system.

The same drug were administered to same patient by dividing then in different group were Old & New cases studied distribution as per Medical history.

**Table 1. Distribution of subjects according to co morbidities**

| S.no | Diseases | No. of patient | Old | New |
|---|---|---|---|---|
| 1 | Chronic cardiac failure | 5 | 3 | 2 |
| 2 | Myocarditis | 10 | 5 | 5 |
| 3 | Chronic Rheumatoid Heart diseases | 20 | 12 | 8 |
| 4 | Ischemic heart diseases | 10 | 6 | 4 |
| 5 | Pericardial effusion | 4 | 2 | 2 |
| 6 | Hypertension | 25 | 15 | 10 |
| 7 | Hypocalcaemia | 6 | 3 | 3 |
| 8 | Coronary arterial diseases | 10 | 8 | 2 |
| | Total | 90 | 54 | 36 |




| | 12-18 years | 19-35 years | 35-50 years | >50 years | Total |
|---|---|---|---|---|---|
| No. of Male | 1 | 2 | 15 | 35 | 53 |
| No. of Female | 1 | 4 | 12 | 20 | 37 |
| Total | 2 | 6 | 27 | 55 | 90 |

**Fig. 2. Showing distribution of study population**

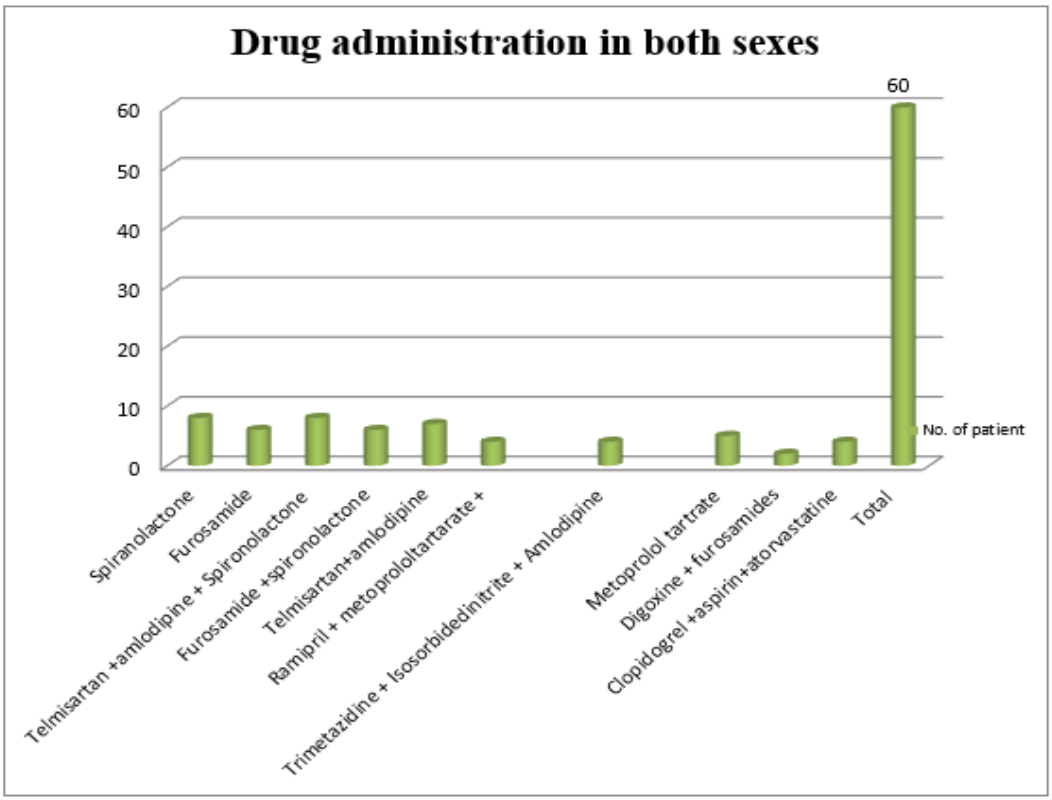



**Fig. 3. Drug administration in both sexes**

On the basis of sex involved on maximum drug used were furosemide and spironolactone in female 5, in male 4. Digoxin, furosemide and spironolactone was about 70.58% of total ADRs attained from these combinations. Drug administered in male and female sex is discussed in Fig. 3 where Table 1 discussed patient number with various diseases.

**Table 2. ADRs % with a single and combination therapy on the basis of disorders ,drug used for their co morbidities**

| S.no | Drug | Disorder | Major Clinical symptoms | co morbidities | ADRs | ADRs % |
|---|---|---|---|---|---|---|
| 1 | Spironolactone+ Torsemide+ Digoxine | Myocarditis | Cheat pain, | Myocardial infraction | Swelling, headache | 10.52 |
| 2 | 1.Digoxine+clopidogrel+spironolactone +torsemide<br>2.Atorvastatine+ Spironolactone+warferine +Diltiazem. | Chronic Rheumatoid Heart Disorder | Chest pain, 3 day back fever Hypotension | Chronic cardiac failure | Swelling ,headache Hypotension ,fluid disturbances Difficulty in motion pass,systolic dysfunction Stomach pain,sleep Disturbances. | 47.36<br>47.30 |
| 3 | 1.Metoprolol+aspirin+amlodipine+clopidogrel | Ischemic heart diseases | Chest pain+ body pain+problem in body moment | ACS | Sleep Disturbance | 5.2 |
| 4 | Furosemide | Pericardial effusion | Edemadifficulty in breathing | Cardiac tamponed | Hypotension, foot swelling, difficulty in body moments | 15.78 |
| 5 | Amlodipine+ Telmisartan+ | Hypertension | Coronary Arterial Diseases | Hypertension, light fever,pain | Fluid Disturbance | 5.2 |
| 6 | 1.Metprolol+ Bisprolol<br>2.Amlodipine+Clopidogrel+ Diltiazem Aspirin+ | Coronary arterial diseases. | Liver dysfunction | Loss of appetite, Difficulty in motion pass | Swelling<br>Sleep disturbance | 10.52 |
| | | Total | | | | 100 |

**Table 3. Distribution of ADRs according to cardiovascular drug therapy**

| S. no | Drug | ADRs | ADRs% |
|---|---|---|---|
| 1 | Spironolactone + Ramipril | Swelling, Hypotension,<br>Distolic dysfunction | 17.64 |
| 2 | Furosemide | Loss of appetite, Dizziness, insomnia | 17.64 |
| 3 | Furosemide +spironolactone | Hypotension, Electrolyte imbalance,<br>Loss of appetite, Anxiety ,both leg pain,Swelling in ,stomach, appetite ,chest, pain<br>hypotension | 58.82 |
| 4 | Telmisartan+<br>Amlodipine+ Spironolactone | Headache ,rashes ,anxiety, dizziness loss of appetite, urinary tract,<br>Infection,vomiting,constipation, insomnia | 47.05 |
| 5 | Metoprolol tartrate + Amlodipine | Hypotension ,chest pain | 11.76 |
| 6 | Isosorbide nitrite<br>+Amlodipine | Hypertension, sleep disturbance. Anxiety, | 17.64 |
| 7 | Metoprolol tartrate | Stomach pain, swelling | 19.45% |
| 8 | Digoxin+ furosamides+spironolactone | Headache, swelling ,fluid, disturbance,<br>systolic dysfunction, chest pain, appetite<br>hypotension, vomiting, difficulty in breathing, abdominal pain, nausea | 70.58 |
| 9 | Clopidogrel +aspirin+atorvastatine | Anxiety, insomnia,hypertension,headache, | 23.52 |
| | Total | | 100 |

**Table 4. Distribution of ADRs according to body system**

| S.no | Body System | ADRs | ADRs % |
|---|---|---|---|
| 1 | CNS | Vomiting,Nausea,dizziness, insomnia, vomiting,, headache, anxiety ,sleep disturbance | 32.14 |
| 2 | G.I.T | Dyspepsia, Stomach pain, loss of appetite,<br>Difficulty in motion pass, Abdominal pain. constipation | 21.42 |
| 3 | Urinary System | Urinary tract infection ,swelling | 7.14 |
| 4 | Respiratory System | Difficulty in breathing, cough, | 7.14 |
| 5 | Excretory System | fluid,disturbance ,electrolyte imbalance | 7.14 |
| 6 | C.V.S. | Chest, pain ,hypertension, hypotension,Systolic dysfunction. | 14.28 |
| 7 | Others | Skin rushes, Swelling, leg pain | 10.71 |
| | | Total | 100% |

On the basis of disorders drug used for their co morbidities to find out ADRs in which maximum ADRs found in chronic rheumatoid heart diseases, for this diseases patient took in two combination mainly digoxin with clopidogrel (47.36%) and another were with atorvastatin, spironolactone and warfarin 47.30 % of adverse effects which was maximum in compare to other diseases. Patient on combination therapy (Digoxin, Furosemide, and Spironolactone) had significantly more complaints regarding side effects than other category of drugs. The risk of side effects associated with the combination of digoxin was six times higher than Metoprolol. The result obtained in some of previous studies in which Digoxin and Furosemide were well tolerated.

On the basis of Cardiovascular Drug Therapy drug used for their co morbidities to find out ADRs in which maximum ADRs found in Digoxin, furosemide and spironolactone was about 70.58% of total ADRs attained from these combinations.

The distribution of ADRs depicting various social habits imparts the drug interaction feasibilities in patients with both alcohol and tobacco users was observed with the most ADRs (32.14%).

Another aspect on basis of adverse drug reactions on particular body system was the most on CNS. (32.14% ADRs) and next most common were on GIT Were 21.42% out of total ADRs.

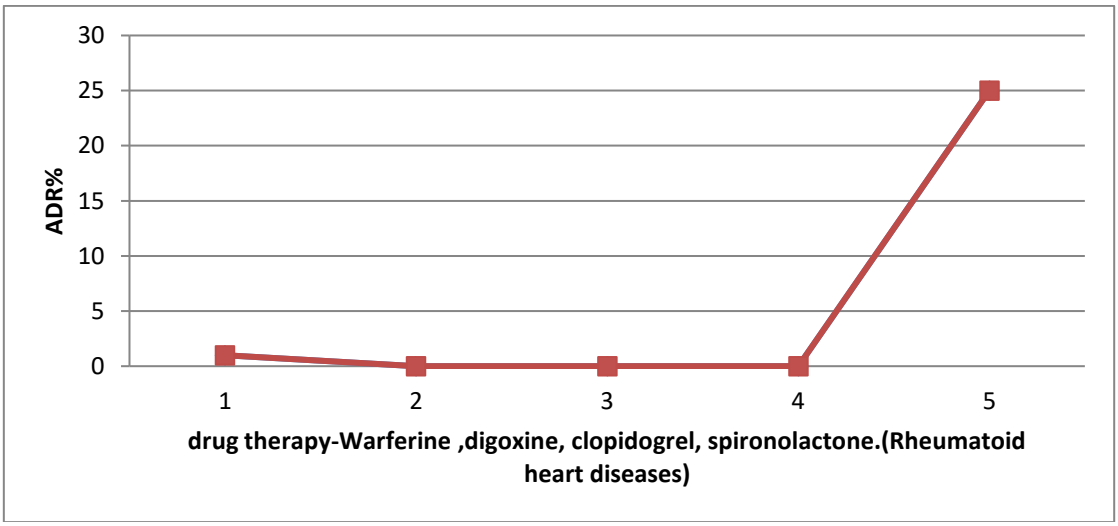



**Fig. 4. Distribution of ADRs as per social habits (tobacco, smoking users)**

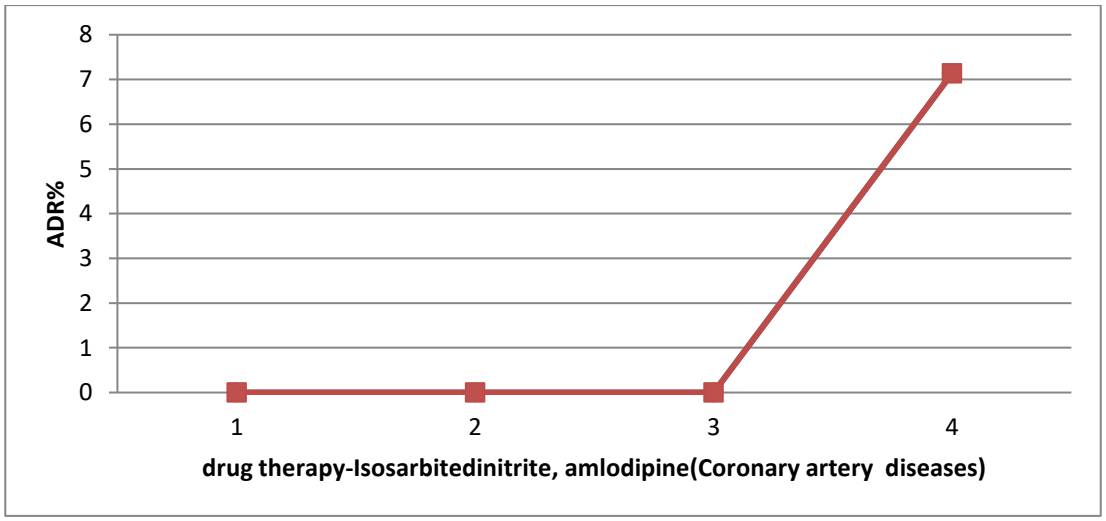



**Fig. 5. Distribution of ADRs as per social habits (smoking users)**

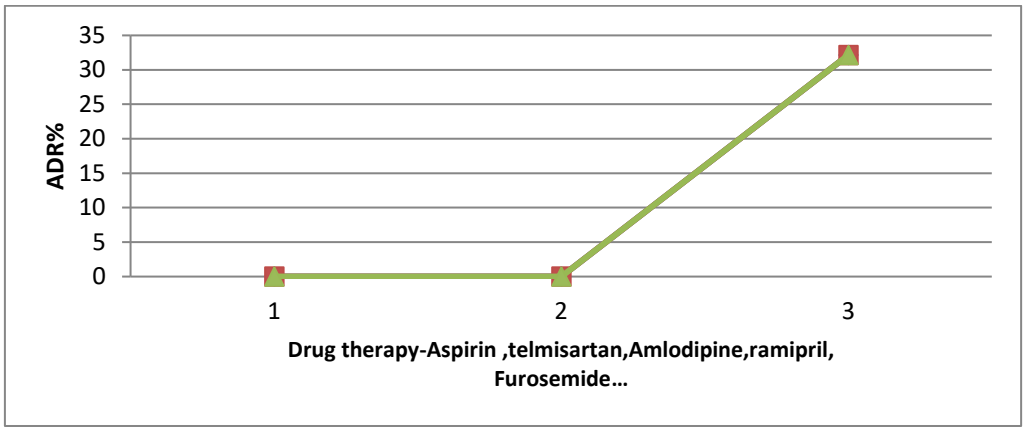



**Fig. 6. Distribution of ADRs as per social habits (Alcohol & tobacco users)**

But there are some variations in the results which show there are some new outcomes in comparisons of the previous data. The most important reason behind these variation does not mean that thesome contradiction in previous studies but indirectly they are in quite support for my study.The side effect experienced by Spironolactone was swelling,hypotension, and systolic dysfunction.

**Table 5. ADR distribution in the preview of Naranjo causality assessment scale**

| S.no | Drug | Nranjo's score | Inference |
|---|---|---|---|
| 1 | AMLODIPINE | 7 | PROBABLE |
| 2 | ATORVASTATINE | 5 | PROBABLE |
| 3 | FUROSEMIDE | 8 | PROBABLE |
| 4 | FUROSEMIDE | 5 | PROBABLE |
| 5 | ISOSARBIDE DINITRITE | 5 | PROBABLE |
| 6 | METOPROLOL | 7 | PROBABLE |
| 7 | RAMIPRIL | 5 | PROBABLE |
| 8 | SPIRONOLACTONE | 6 | PROBABLE |
| 9 | TELMISARTAN | 7 | PROBABLE |
| 10 | TORSEMIDE | 5 | PROBABLE |
| 11 | METOPROLOL | 7 | PROBABLE |
| 12 | DIGOXINE | 6 | PROBABLE |
| 13 | TELMISARTAN | 6 | PROBABLE |

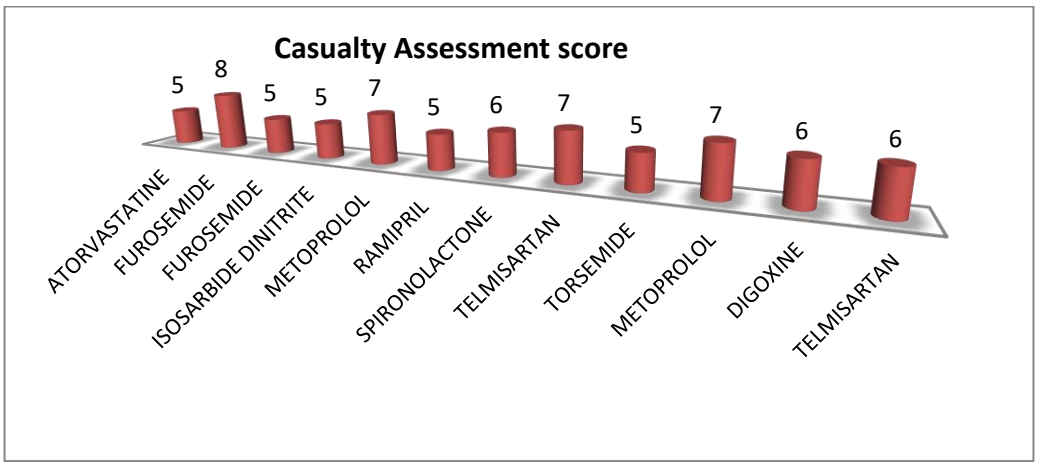



**Fig. 7. ADR distribution in the preview of Naranjo causality assessment scale**

Lastly just after the analysis of all result this was the outcome of whole study was seen according to Naranjo scale we found that the maximum possible and probable adverse drug reaction were shown on Furosemide as well as for Digoxin, Spironolactone too.it was also be very clearly appreciated in Table 4 & Fig. 7.

## 4. DISCUSSION

After the data was thoroughly analyzed, it was discovered that there were several differences between the data and the prior data, which led to an extremely unexpected conclusion. Regarding the result's explanation, roughly 40–50% of the results are entirely consistent with the prior body of information. As it is already known that if the data which I have collected fulfils about 50% then it demonstrates that there are many parallels with the already released data which is already shown in the references.Last but not least, following a thorough review of all the data, we discovered that shown on furosemide had the most likely and largest potential for a negative medication reaction. This was determined using the Naranjo scale were same applicable in digoxin, spironolactone.
too.

## 5. CONCLUSION AND PERSPECTIVES

It may be inferred that while all three medications were well tolerated, furosemide, spirolactone, and digoxine exhibited a greater number of adverse effects. ADRs frequently contribute to sickness in the elderly, according to assessments of this population. It is necessary to take a closer look at these ADRs, and improving intervention will undoubtedly boost patient and medication compliance. For that reason, this study established baseline data for larger studies to come and determined the significance of prospective ADRs surveillance in pharmacovigilance research.

## DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

## CONSENT

As per international standards or university standards, Participants' written consent has been collected and preserved by the author(s).

## ETHICAL APPROVAL

The study was conducted after receiving approval from Ethics Committee (Reference number-IEC/2024/4355.)

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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